(19) World Intellectual Property Organization

International Bureau



(43) International Publication Date 23 December 2004 (23.12.2004)

PCT

(10) International Publication Number WO 2004/110451 A1

(51) International Patent Classification⁷: A61P 25/04, A61K 31/485, 31/4468

A61K 31/496,

(21) International Application Number:

PCT/EP2004/051050

(22) International Filing Date:

7 June 2004 (07.06.2004)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: PCT/EP03/06118

10 June 2003 (10.06.2003) EP

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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(54) Title: COMBINATIONS FOR OPIOID-BASED TREATMENT OF PAIN COMPRISING 1-(1,2-DISUBSTITUTED PIPERIDINYL)-4-SUBSTITUTED PIPERAZINE DERIVATIVES

$$\begin{array}{c|c}
R^1 \\
Q \\
N \\
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(CH_2)_m \\
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(CH_2)_p
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(I)

(57) Abstract: This invention concerns novel formulations for opioid-based treatments of pain and/or nociception comprising opioid analgesics and 1-(1,2-disubstituted piperidinyl)-4substituted piperazine derivatives having neurokinin antagonistic activity, in particular NKI antagonistic activity the use of said formulation for the manufacture of a medicament for the prevention and/or treatment of emesis, pain and/or nociception, in particular

in acute and chronic pain treatments, more in particular in inflammatory, postoperative, emergency room (ER), breakthrough, neuropathic and cancer pain treatments and the use of an NKI-receptor antagonist for the manufacture of a medicament for the prevention and/or treatment of respiratory depression and tolerance in opioid-based treatments of pain. The pharmaceutical formulations according to the invention comprise NK₁- antagonists according to the general Formula (I) the pharmaceutically acceptable acid or base addition salts thereof, the stereochemically isomeric forms thereof, the N-oxide form thereof and prodrugs thereof, wherein all substituents are defined as in Claim 1. The pharmaceutical composition according to the invention reduces to a large extent a number of unwanted side-effects associated with opioid analgesics, in particular respiratory depression and tolerance, thereby increasing the total tolerability of said opioids in pain treatment.



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IT. LU. MC. NL, PL, PT. RO. SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

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- of inventorship (Rule 4.17(iv)) for US only

Published:

with international search report

 before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

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